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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/072,185	02/08/2002	Shih-Jen Liu	13886-002001 / 01P0325	3503

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EXAMINER	
SZPERKA, MICHAEL EDWARD	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 11/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/072,185	LIU ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *1-17 and 28-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/5/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Group IV, a composition comprising a carrier, antigen presenting cells, and a heat shock fusion protein wherein the heat shock protein is HSP70 and the fused antigen is prostate specific antigen (PSA) from the disease prostate cancer, in the reply filed on October 8, 2004 is acknowledged.

Claims 1-35 are pending in the current application.

Claims 1-17 and 28-35 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

Claims 18-27 are under examination in the instant application as they read on the elected heat shock fusion protein species of HSP70, PSA, and prostate cancer.

Specification

2. The disclosure is objected to because of the following informalities:

It appears that everywhere in the specification that a temperature is indicated, there is a formatting problem with the symbols for degrees Celsius (^{0}C). For example, on page 7, line 11, the temperature for the incubation of *E. coli* is indicated as 37 followed by a box.

Appropriate correction is required.

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 18, 21, 23, 24, and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant has claimed the broad genus of fragments of polypeptides when only the species of PSA and AFP fragments are disclosed. Applicant has also claimed fusion proteins that encompass heat shock proteins in addition to HSP70. The broadest reasonable interpretation of the claims indicates that fusions can be created with domains of any heat shock protein (HSP) while the only fusion disclosed contains the C-terminal region of HSP70. The structure and function of such fusion proteins has not been disclosed, nor has a relationship been structure and the resulting function been established. MPEP section 2163.05 clearly states that when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

As indicated above, there is substantial variation within the claimed genus

of heat shock fusion proteins and fragments of oncogenes and tumor suppressor genes. Since there is high variability amongst the genus of polypeptides of the claimed invention, and Applicant has disclosed only the species fusions containing HSP70 and the antigens PSA and AFP, the claimed invention does not have written support within the originally filed specification. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, § 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, which make clear that if a claimed genus does not show actual reduction to practice for a representative number of species, then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 18-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srivastava (U.S. Patent No. 5,985,270, see entire document) in view of Suzue et al. (Journal of Immunology, 1996, 156:873-879, see entire document).

Srivastava teaches a composition comprising purified dendritic cells, HSP70, the prostate cancer antigen PSA, and a pharmaceutically acceptable carrier (see particularly the paragraph that spans columns 2 and 3, lines 11-17 of column 3, lines 26-29 of column 4, lines 57-62 of column 5, lines 5-26 of column 6, lines 48-50 and 57-58 of column 13, lines 23-49 of column 16, and claims 21-23). These teachings differ from the claimed invention in that the antigen, PSA, is not covalently linked to HSP70 to create a heat shock fusion protein.

Suzue et al. teach a vector system that permits the production of any HSP70 fusion protein, and demonstrate the advantages of such a system by characterizing the use of a heat shock fusion protein that covalently links HIV-1

p24 to HSP70 (see entire document, particularly the abstract, the Materials and Methods section titled expression vector constructs that begins on page 873, and the first full paragraph of the right column of page 877). They observed that the covalent linkage of p24 to HSP70 was essential to eliciting an immune response in the absence of adjuvant, and that fusing an antigen to HSP70 obviates the need for an exogenous adjuvant (see particularly Figure 4 and the first paragraph of the discussion on page 877). HSP70 fusion proteins have the additional advantages of being easy to produce in large amounts, to purify and to characterize. The number and position of potential epitopes are identical for each heat shock fusion molecule, a property not shared by other heat shock protein compositions, including those taught by Srivastava et al., that use heat shock proteins as an antigen carrier (see particularly the first full paragraph of the right column of page 877). This homogeneity of heat shock fusion proteins is an advantage that reduces variability associated with the use of heat shock proteins as immunological carriers because immune responses can be strongly affected by differences in the molar ratio between the antigen and carrier (see particularly the final two sentences of the first full paragraph of the right column of page 877).

Therefore, one of ordinary skill in the art at the time of the invention would have been motivated to modify the teachings of Srivastava to include a heat shock fusion molecule consisting of HSP70 and PSA because of the heat shock fusion protein advantages of production, purification, characterization, lack of a need for exogenous adjuvant and homogeneous antigen to carrier ratio which

minimizes interexperimental variability in immune responses as taught by Suzue et al.

7. Claims 18 and 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Srivastava (U.S. Patent No. 5,985,270, see entire document) in view of Suzue et al. (Journal of Immunology, 1996, 156:873-879, see entire document) as applied to claims 18-23 above, and further in view of Tong et al. (Cancer Research, 2001 61:7530-7535, see entire document).

The teachings of Srivastava and Suzue et al. have been discussed above. These teachings differ from the claimed invention in that they do not disclose the use of cytotoxic compounds, such as chemotherapeutic agents, with a composition consisting of dendritic cells, heat shock fusion proteins, and a pharmaceutically acceptable carrier.

Tong et al. disclose the use of systemic chemotherapy in addition to the administration of dendritic cells in mouse tumor models (see particularly the abstract). Mice received injections of the antitumor agent CTX and dendritic cells on days 12 and 14 of the experimental protocol, and were compared to mice that received no treatment, just dendritic cells or just CTX (see particularly the Materials and Methods section titled Combined Intratumoral DCs and Chemotherapy on page 7531, left column, Figures 1 and Figure 2). Their data indicate that the most dramatic antitumor effects are seen when the administration of dendritic cells is combined with systemic chemotherapy, such a combination leading to the advantages of marked tumor suppression and

persistent antitumor immune memory (see particularly Figure 1, Figure 2, the second full paragraph of the right column of page 7530, and the first paragraph of the Discussion on page 7534). Tong et al. further indicate that their strategy is broadly applicable to the treatment of other tumors (see particularly the paragraph that spans pages 7534 and 7535).

It would have been obvious to one of ordinary skill in the art at the time of the invention to include a chemotherapeutic agent with a composition comprising dendritic cells and a heat shock fusion protein based on the successful use of dendritic cell administration and chemotherapy to cause tumor regression in an animal model as taught by Tong et al. Motivation to do so comes from the teaching that chemotherapy combined with dendritic cell administration is more effective in treating tumors that dendritic cell administration alone, (see particularly Figure 1, Figure 2, the first full paragraph of the left column and the last full column of the right column of page 7534, and the paragraph that spans pages 7534 and 7535).

8. No claims are allowable.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is 571-272-2934. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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October 29, 2004

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